capable of inducing HLA-A2 restricted cytotoxic T cells in a bulk culture, i.e., to contain a T-cell epitope presented with HLA-A2 (M.R. Wills et al. (1996), J. Virol. Vol. 70, pp 7569-5779). The length of 9 amino acids for the fragments to be tested was chosen because this is the typical length of epitopes presented with MHC class I molecules (H.G. Rammensee et al. (1995), Immunogenetics, Vol. 41, pp 178-228). The peptides used respectively overlap by 8 amino acids, for successive peptides, and thus comprise all possible fragments of this length. The peptides were employed as a mixture of all peptides or singly. The peptide concentration in the Example shown was 1 µg/ml for each peptide.

The following peptides were employed:

1) Ala Arg Asn Leu Val Pro Met Val Ala [SEQ ID NO.:2]
2) Arg Asn Leu Val Pro Met Val Ala Thr [SEQ ID NO.:3]
3) Asn Leu Val Pro Met Val Ala Thr Val [SEQ ID NO.:4]
4) Leu Val Pro Met Val Ala Thr Val Gln [SEQ ID NO.:5]
5) Val Pro Met Val Ala Thr Val Gln Gly [SEQ ID NO.:6]
6) Pro Met Val Ala Thr Val Gln Gly Gln [SEQ ID NO.:7]
7) Met Val Ala Thr Val Gln Gly Gln Asn [SEQ ID NO.:8]

Incubations with the mixture of all peptides (Figure: upper left diagram) and with peptide 3 alone (Figure: middle column, second diagram from above) resulted in the production of IFN-γ in T cells, detected by measurement in a flow cytometer on the individual cell level (J.L. Picker et al. (1995), Blood, Vol. 86, pp 1408-1419). None of the other individually tested peptides had this effect. A study published in the literature identified exactly the same epitope within the same protein segment by conventional methods and clearly confirms our result (D.J. Diamond et al. (1997), Blood, Vol. 90, pp 1751-1767).

Legend for Figure 1/2:

Detection of intracellular interferon-γ in $CD8^+$ T lymphocytes after stimulation with a mixture of the 7 peptides stated (upper row, leftmost diagram) or the individual peptides, $pp65_{493-501}$ to $pp65_{499-507}$. The marker CD69 was used as an activation marker. The representation is limited to $CD3^+/CD8^+$ events, and the average fluorescence intensity is stated.

Example 2

(see Figure 2)

Mononuclear cells were prepared from the peripheral blood, obtained by venous punction, of an HLA-typed female patient possessing the MHC class II allele HLA-DR11. The patient additionally possessed antibodies against human cytomegalovirus. The cells prepared by a standard method were incubated with mixtures of 11 or 12 peptides each having a length of 15 amino acids with 11 overlaps respectively, corresponding to the sequence of the pp65 matrix phosphoprotein (Swiss-Prot PO6725), for six hours under optimized conditions (a total of 138 peptides). [SEQ ID NO.:1] The peptide concentration was 1 µg/ml for each peptide. Three out of a total of 24 mixtures clearly stimulated $CD4^+$ T cells. Due to the experimental design (occurrence of particular peptides in particular mixtures), 2 peptides could thus be clearly identified which were responsible for the stimulation. This result was confirmed by the stimulation with the respective individual peptides under otherwise equal conditions. The identified peptides were the neighboring peptides $pp65_{365-379}$ and $pp65_{369-383}$. These sequences are largely congruent with the following HLA-DR11-presented peptide sequences described in the literature, which were identified as T-cell stimulating sequences in the conventional way: $pp65_{361-376}$ and $pp65_{369-384}$ (Khattab et al. (1998), Journal of Medical Virology, Vol. 52, pp 68-76), i.e., the stimulating peptides are found within the segment defined by the amino acids 361 and 384. A further narrowing down of the epitope sequence to the postulated length of 11 amino acids has not been done.

Legend for Figure 2/2:

Detection of intracellular interferon-γ in $CD3^+/CD8^-$ T lymphocytes (left) after stimulation with the peptide mixtures 8, 9 and 20, or in $CD3^+/CD4^+$ T lymphocytes (right) after stimulation with the individual peptides $pp65_{365-379}$ and $pp65_{369-383}$. In the screening (right), peptide mixtures were used, and CD3 and CD8 were used as T cell markers. Since the $INF\text{-}\gamma^+$ populations on the left side are $CD3^+/CD8^-$, the marker CD4 was used for retesting. The stimulated T cells are clearly $CD4^+$. Only $CD3^+$ cells are shown, and the average fluorescence intensity is stated.